STUDIES ON LIVER FRUCTOKINASE

BY

NORMAN HOWARD GRANT

Ph.B., University of Chicago, 1946
S.B., University of Chicago, 1947
M.S., University of Illinois, 1948

AN ABSTRACT OF A THESIS

SUBMITTED IN PARTIAL FULFILLMENT OF THE REQUIREMENTS
FOR THE DEGREE OF DOCTOR OF PHILOSOPHY IN
CHEMISTRY IN THE GRADUATE COLLEGE OF
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R. UNIV. BIBLIOTHEEK LEIDEN

STUDIES ON LIVER FRUCTOKINASE

INTRODUCTION

An earlier study in this laboratory revealed that glucose was not readily utilized by rat liver homogenates and slices. Fructose was found to be taken up easily. In view of the established importance of glucose in intermediary metabolism, the apparent lack of phosphorylation under these conditions was puzzling. The most cogent explanations were (1) reversal of the phosphorylation by potent phosphatase action; (2) the use of a system unsatisfactory for glucose phosphorylation; and (3) the absence of an active liver glucokinase. The present investigation was designed, in part, to study these possibilities.

The central role of fructose phosphates in the glycolytic scheme, the easy phosphorylation of fructose by liver and the uncertainty surrounding insulin action all pointed to the need for a further study of liver fructokinase. The end-products of fructose phosphorylation and liver fructokinase activity in alloxanized and insulinized rats were therefore investigated.

EXPERIMENTAL

Hexokinase activity was measured by the disappearance of hexose. Phosphatase activity was measured by the appearance of free hexose reducing power. The complete system contained magnesium chloride, sodium glutamate, potassium phosphate buffer, liver homogenate (or slice), ATP and hexose. After incubation, changes in reducing power were determined by the method of Nelson (1) and fructose by the method of Roe (2). The fractionation procedure outlined in Umbreit *et al.* (3) was employed for analyzing hexose phosphates. The results of the diabetes study were treated statistically.

SUMMARY OF RESULTS

1. Phosphatase activity was not great enough to explain the apparent lack of glucose phosphorylation by liver homogenates.

2. The addition of brain hexokinase to the above system allowed a phosphorylation of glucose to an extent comparable to that of fructose. The combination of brain extract and liver homogenate possessed glucokinase activity greater than the sum of the two studied separately.

3. Phosphoenolpyruvate was not able to transfer a phosphate group to glucose or fructose.

4. The conversion of glucose to fructose in fructokinase-blocked systems could not be demonstrated.

5. There is an accumulation of the first end-product of fructose phosphorylation (presumably fructose-1-phosphate) after one-half hour of incubation. Fructose-6-phosphate is quite rapidly metabolized.

6. The livers of alloxan-diabetic male rats show fructokinase activities about half those of normal male and normal and alloxanized female rats.

7. The livers of alloxan-diabetic male rats maintained on insulin show fructokinase activities somewhat greater than those of normal rats.

8. The livers of castrated male rats, three of which were given estrogen, show essentially normal fructokinase activity.

9. The results suggest the following tentative interpretation: In the male rat there is more alloxan liver cell damage than in the female. The administration of insulin to the male alloxanized rat or the absence of androgens in the male alloxanized castrate rat leads to apparent repair of liver systems and normal fructokinase activity.

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VITA

The author was born in Chicago, Illinois on July 21, 1927. He attended public schools there, and, following graduation from Von Steuben High School in June, 1944, he entered the University of Chicago. He received the degree of Bachelor of Science in June, 1947. He was employed at the Plymouth Laboratories in Chicago from June, 1947, until he entered the Graduate College of the University of Illinois in October, 1947. In August, 1948, he received the degree of Master of Science. In the Fall of 1949, he held a half-time teaching assistantship. From September, 1948, to September, 1949, and February, 1950, to September, 1950, he held an Atomic Energy Commission Predoctoral Fellowship in the Biological Sciences, administered by the National Research Council.

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